Sensory information from afferent neurons

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QUARTERLY PROGRESS REPORT #1

for the period

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I. Objectives of Overall Project

In this newly awarded research contract we will build on the work done in the initial 3-year contract (NO1-NS-3-2380). Our aim is to develop and perfect, in an animal model, methods for chronic recording and processing of afferent activity produced by sensory receptors that could yield information about human fingertip contact, grasped object slip, finger position, and grasp force applicable for restoration of motor functions in the paralyzed human hand. The specified contract objectives are:

1. Select recording methods that:
   a. Have the potential of providing safe, reliable recordings in humans for periods of years.
   b. When used in human applications, could provide relatively isolated information from the sensory endings in the thumb pad and in the finger pads of the second and third fingers.
   c. Could, in human applications, provide information from the proprioceptive receptors in the muscles of the hand and wrist.

2. Select an animal model suitable for chronic recording of afferent nerve activity, and give consideration to modeling electrode placement sites for a potential human neural prosthesis application.

3. Fabricate or obtain chronic electrodes and associated cables and percutaneous connectors for chronic recording of sensory afferent activity.
   a. Design electrodes and cables using biocompatible materials that would be suitable for potential future human implants.
   b. Design electrodes and cables with the goal of producing a chronic implant that causes minimal nerve damage.

4. Investigate the possibility of extracting information about contact, grasped object slip, limb position and contact force from chronically recorded neural activity using the animal model and electrodes from parts 2 and 3.
   a. Devise recording, processing, and detection methods to extract this information from recorded neural activity in a restrained animal.
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation.
   c. Record activity for periods of at least 6 months and devise functional measures to track any change in neural response over this time.
   d. Evaluate any histological changes in the nerves that occurred over the period of chronic recording and, if possible, correlate these changes to changes in functional response.

5. Cooperate with other investigators in the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Progress in the First Quarter

The research for our preceding contract was centered on the use of tripolar nerve recording cuffs (Hoffer, 1990; Strange et al., 1995) implanted on the median, ulnar and radial nerves in the forearm, and thus a single channel of information was recorded from each cuffed nerve. The sensory endings in the thumb pad and in the finger pads of the second and third fingers are innervated by two main digital nerve branches per finger, belonging to the median and/or ulnar nerves. To address Objective 1 of the current contract, two basic approaches can be envisioned. To obtain multiple channels of information, up to six small nerve cuffs could be implanted around the individual digital nerve branches in the fingers or palm of the hand. A palmar location was recently tested for one digital nerve in two volunteers by the Aalborg group (Haugland et al., 1995; Slot et al., 1995). To implant multiple cuffs would require considerable surgical time and, generally, the smaller the nerve, the greater the risk of injuring it by installing a cuff (Hoffer, 1990). The second approach is to attempt to record several channels of information from larger nerve trunks situated more proximally, e.g., in the forearm region. This way, surgical access is simpler and faster and the viability of the larger nerves may be less compromised. Because of its potentially greater potential for clinical implementation (Objective 1), we have chosen this approach for our proposed research. Cat forelimb nerves have been selected as the model system, because of their similar size to human digit nerves and similar function to human forearm nerves, as well as the trainability of cats for producing repeatable movement tasks with the forelimb.

In the first quarter we have started to develop and test two alternative recording methods that are expected to provide multiple channels of sensory information from the main nerves in the forearm: **multicontact nerve cuffs** and **intrafascicular electrodes**. These approaches will be described below. As well, we began to develop a **digit manipulator** with which we will explore and characterize nerve signals recorded in response to cutaneous stimulation.

Multicontact nerve cuffs

Multicontact nerve cuffs have been used in recent years for selective stimulation of subpopulations of axons in a nerve trunk, e.g., using novel methods for "steering" the stimulation current impulses between two or more electrodes (Veraart et al., 1993). The approach we intend to use is in some respects the converse of selective stimulation: we aim to design cuff electrode configurations and signal analysis methods that will render selective recordings of the nerve impulse traffic generated by different sensory nerve fiber groups and/or occurring in different regions of a nerve trunk enclosed within the cuff.

There are few theoretical or experimental studies in the literature that address the possibilities and expected limitations of multichannel nerve cuff recordings. For afferent axons individually activated in the saphenous nerve of the cat, different action potential signatures could sometimes be recorded by separate tripolar electrode sets placed within a femoral nerve cuff (Hoffer et al., 1981), suggesting that high electrode selectivity is in principle feasible. A review of several possible recording approaches was published by Hoffer and Haugland (1992). The abstracts for two upcoming conference communications (Sahin et al., in press; Struijk et al., in press) report attempts at obtaining selective recordings from nerve branches using multicontact nerve cuffs, where only very modest selectivity was obtained. Although the multicontact approach may at first appear fairly straightforward, it is apparent that in order for high selectivity to be obtained, the electrode configurations and signal analysis methods must be carefully designed and optimized.

During the first quarter we started to investigate novel designs for multicontact cuffs in acute cat experiments and obtained very encouraging initial experimental results. Cuffs were made of silicone, contained several electrodes arranged in a specific pattern, and implemented our improved cuff opening and closing technique (Kallesøe et al., 1996). The experimental model consisted of a multicontact cuff placed around the sciatic nerve of the cat. Upon electrical stimulation of each of five nerve branches (common peroneal, lateral gastrocnemius/soleus, medial gastrocnemius, sural and distal tibial) the resulting nerve compound action potentials had markedly different amplitudes and shapes when different recording electrode configurations were used, such that the activation of particular nerve branches gave much larger signals in some electrodes than in others, and different electrodes showed the largest signals when other nerve branches were stimulated. These results are very preliminary and thus will not be reported in further detail here. We are currently continuing to better understand the key parameters that can lead to improved selectivity using nerve cuffs for multichannel recordings.

Multiunit intrafascicular electrodes

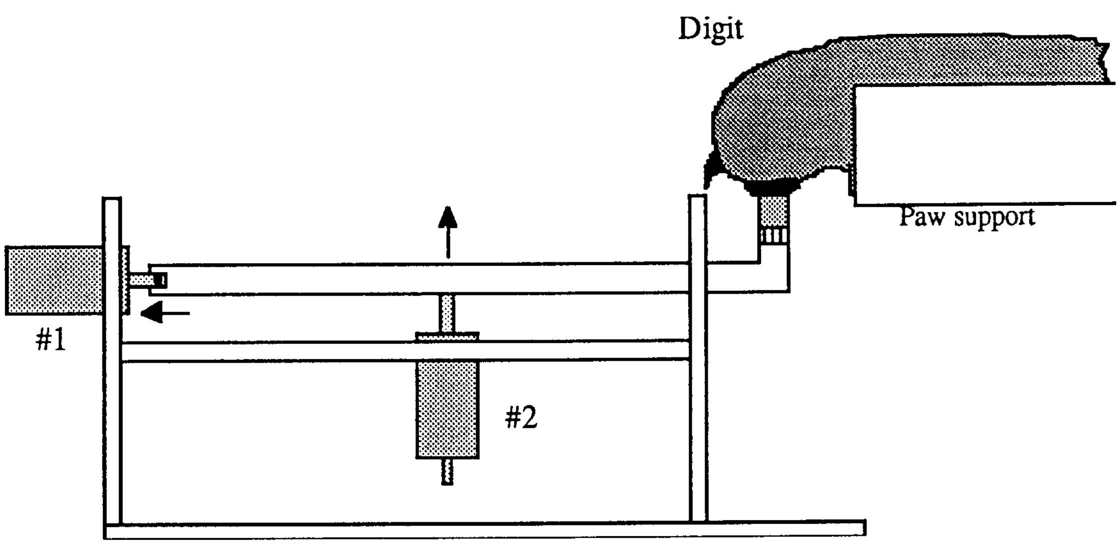
Multiunit intrafascicular electrodes were used to record the activity of muscle afferent populations in a hindlimb muscle nerve in acute experiments in anesthetized or decerebrate cats (Yoshida and Horch, 1996). Although the surgical installation time and risk of causing chronic damage to nerves can both be expected to be higher than when using a nerve cuff, intrafascicular electrodes may provide higher selectivity than multicontact cuffs. In this research we intend to investigate the recording selectivity properties and longevity in the chronic preparation. As per the specifications of this contract, both the intrafascicular electrodes and the multicontact nerve cuffs, cables and implanted hardware must be suitable for recording nerve signals that are stable during movement and invariant for at least 6 months. The intrafascicular electrodes will be supplied by K. Yoshida and R.B. Stein as Subcontractors and will be implanted at SFU, where we will contrast these results with results from multicontact cuffs implanted on the same nerves. In the first quarter, we have initiated the formulation of intrafascicular electrode characteristics that will be delivered in the next quarter.

Digit Manipulator

To address Objective 4 of the contract we are developing a model system in which to compare and contrast signals recorded with single nerve cuffs, multicontact cuffs and intrafascicular electrodes. In the First Quarter we started experiments under anesthesia to study information present in the median, ulnar and radial nerves that reflects touch and slip in forepaw digits.

The digit manipulator is a device capable of producing mechanical perturbations, including tangential slips (Haugland and Hoffer, 1994) and calibrated perpendicular indentations (Haugland, Hoffer and Sinkjær, 1994) to individual forepaw digit pads of a cat while under anesthesia. These perturbations cause activity in sensory fibres, both proprioceptive and cutaneous, which is recorded by nerve cuff or intrafascicular electrodes. The final version of the digit manipulator will have five independent probes aligned under the forepaw, with one probe under each digit that will cause perturbations in each of two dimensions.

In the First Quarter a single-digit manipulator was constructed by P. Christensen, that is capable of perturbing a digit in each of two dimensions (see Figure, below). Solenoids are used in this design because they are easy to control and are relatively inexpensive. The magnitude of the applied perturbation is controlled by limiting solenoid return to the resting position. For slip perturbations, a return spring and hard stop are utilized. For calibrated perpendicular indentations, blocks are used to stop the return of the piston in the vertical solenoid.



Solenoid #1 is a pull-type solenoid that is responsible for slip perturbations. When it is energized, the tip of the manipulator is pulled across the digit pad, thus creating a tangential slip. Although not shown in the figure, a return spring is used to pull the manipulator's lever arm out of the solenoid and back against a hard stop. The position of the hard stop can be changed to control the length of the slip perturbation.

Solenoid #2 is a push-type solenoid that is responsible for the perpendicular perturbation against the digit pad. When it is energized, the piston pushes up the lever arm of the manipulator. Because the solenoid is located about half way along the lever arm, the end of the arm travels twice the distance of the piston. This is a good configuration for a solenoid since the shorter the stroke length of the piston of the solenoid, the greater the force it may generate. However, the amount of end point force is also limited to half of the force generated by the solenoid.

In the future, a multi-digit manipulator capable of perturbing any one of the digits in any order or mode will be developed. This design will be an extension of the current single-digit manipulator although some considerations about size of components, positioning of the manipulator arms, and control issues still need to be addressed. More advanced features like full force and position control of the perturbations will be added if needed.

The specifications of the current single-digit 2-D manipulator are as follows:

solenoid force (at 6 mm stroke length):	2 N
end-point displacement (maximum):	12 mm
power:	36W (12 V, 3A), DC power
size (LxHxW):	approximately 15 cm x 8 cm x 3 cm

Extraction of sensory features with machine learning techniques

To further address Objective 4 as this research evolves, we will deploy a variety of analytical approaches, including machine learning and adaptive logic networks, to extract sensory information from recorded nerve signals. To this end, A. Kostov and B. Andrews will be collaborating as Subcontractors. In a preliminary collaboration with A. Kostov, we have applied machine learning and adaptive logic networks approaches to data collected from walking cats in the previous contract (Kostov et al., 1996). This approach will form a basis for our planned studies utilizing data to be collected in the present project.

IV. Plans for the Second Quarter

A. We will implant multichannel cuffs in additional acute cats in order to test and compare methods that are expected to further improve their selectivity. This aspect will be carried out primarily by K. Strange, J.A. Hoffer and Y. Chen with assistance from T. Blasak.

B. We will continue with the design and construction of hardware and control software for experiments to explore cutaneous fields in cat digit pads recorded under anesthesia. This work will be carried out primarily by P. Christensen, Y. Chen and J.A. Hoffer.

C. Once the best multicontact cuff design is selected, we will fabricate multicontact nerve cuff electrodes suitable for chronic implantation in median and ulnar nerves of cats. This part of the project will be carried out by K. Strange and Y. Chen under supervision by J.A. Hoffer.

D. We will complete our specification for intrafascicular electrodes suitable for implantation in the same nerves as in part C. The intrafascicular electrodes will be provided by K. Yoshida and R.B. Stein as subcontractors, before the end of the second quarter. Dr. Yoshida will travel about once per quarter to SFU for one week.

E. We will begin to analyze methods to extract contact force and slip information in the acute and chronic experiments under anesthesia. This part of the project will be carried out by P. Christensen, Y. Chen, J.A. Hoffer and K. Strange.

F. We will initiate joint research aspects with A. Kostov and B. Andrews, who will travel to SFU for a week to participate in recordings and collect initial data for analysis.

G. We will train five cats on forelimb postural and locomotory tasks. This will be carried out primarily by the animal health technician, T. Blasak, under supervision by J.A. Hoffer and K. Strange.

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